

**AMENDMENTS TO THE CLAIMS**

Please amend claims 1-2 and 30, cancel previously withdrawn claims 42-53, and add new claims 54-64, as shown in the following listing of claims, which will replace all prior versions and listings of claims in the application. Please cancel previously withdrawn claims 42-53 without prejudice to their pursuit in an appropriate divisional or continuation application. Claims 14-28 and 32-41 are withdrawn. Claims 1-13, 29-31, and 54-64 are currently in the application.

**Listing of claims:**

1 (currently amended). A method for the production of cell cycle specific differentiated hematopoietic cells comprising:

a) culturing purified bone marrow stem cells for cycle initiation from resting state under conditions that promote synchronous progression through the cell cycle;

b) selecting at least one desired cell cycle specific hematopoietic cell type to be differentiated from the synchronous purified bone marrow stem cells upon contact with at least one growth factor or cytokine at a phase of the cell cycle favoring a specific differentiation pathway for the at least one desired cell cycle specific hematopoietic cell type;

c) determining the phase of the cell cycle favoring the specific differentiation pathway for the at least one desired cell cycle specific hematopoietic cell type, and selecting the at least one growth factor or cytokine to promote the specific differentiation pathway or to produce a plurality of cells of the at least one desired cell cycle specific hematopoietic cell type to be differentiated from the synchronous purified bone marrow stem cells upon with at least one growth factor or cytokine at a phase of the cell cycle with the at least one growth factor or cytokine at the pre-determined phase of the cell cycle;

[[b)]d) contacting the synchronous purified bone marrow stem cells with the at least one growth factor or cytokine at [[a)]the predetermined phase of the cell cycle; and

[[c]]e) subculturing the cells until cell cycle specific differentiated hematopoietic cells are produced, wherein a plurality of the cell cycle specific differentiated hematopoietic cells have the at least one desired cell cycle specific hematopoietic cell type.

2 (currently amended). The method of claim 1, wherein the at least one growth factor or cytokine comprises G-CSF, GM-CSF, or steel factor.

3 (previously presented). The method of claim 1, wherein culturing the cells under conditions that promote synchronous progression through the cell cycle comprises culturing the cells in the presence of steel factor, thrombopoietin, and FLT3-ligand.

4 (previously presented). The method of claim 1, wherein the step of subculturing the cells is carried about for about 14 days.

5 (previously presented). The method of claim 1, wherein the predetermined phase of the cell cycle is mid-S phase.

6 (original). The method of claim 5, wherein mid-S phase occurs about 32 hours after initiation of the culturing of the stem cells under conditions that promote synchronous progression through the cell cycle.

7 (previously presented). The method of claim 1, wherein the differentiated hematopoietic cells comprise megakaryocytes.

8 (previously presented). The method of claim 1, wherein the differentiated hematopoietic cells comprise platelets.

9 (previously presented). The method of claim 1, wherein the differentiated hematopoietic cells comprise proliferative granulocytes.

10 (previously presented). The method of claim 1, wherein the predetermined phase of the cell cycle is late S phase.

11 (original). The method of claim 10, wherein late S phase occurs about 40 hours after initiation of the culturing of the stem cells under conditions that promote synchronous progression through the cell cycle.

12 (previously presented). The method of claim 1, wherein the differentiated hematopoietic cells comprise mature (non-proliferative) granulocytes.

13 (previously presented). The method of claim 1, further comprising isolating the differentiated hematopoietic cells from the subculture.

14 (withdrawn). A method of treating a subject having cytopenia comprising administering to the subject a therapeutically effective amount of the differentiated hematopoietic cells produced according to the methods of claim 1.

15 (withdrawn). A method of preventing cytopenia in a subject comprising administering to the subject a therapeutically effective amount of the differentiated hematopoietic cells produced according to the methods of claim 1.

16 (withdrawn). The method of any one of claims 14-15, wherein the subject has or is at risk for developing cytopenia associated with cancer chemotherapy or radiation therapy.

17 (withdrawn). The method of any one of claims 14-15, wherein the subject has or is at risk for developing cytopenia associated with a bone marrow transplant.

18 (withdrawn). The method of any one of claims 14-15, wherein the cytopenia is thrombocytopenia.

19 (withdrawn). The method of any one of claims 14-15, wherein the cytopenia is granulocytopenia.

20 (withdrawn). Hematopoietic cells produced by the methods of any one of claims 1, 14, or 15.

21 (withdrawn). The hematopoietic cells of claim 20, which are macrophages.

22 (withdrawn). The hematopoietic cells of claim 20, which are platelets.

23 (withdrawn). The hematopoietic cells of claim 20, which are proliferative granulocytes.

24 (withdrawn). The hematopoietic cells of claim 20, which are mature (non-proliferative) granulocytes.

25 (withdrawn). A method for the production of differentiated hematopoietic cells comprising:

- a) culturing bone marrow stem cells under conditions that promote synchronous progression through the cell cycle;
- b) contacting the cells with at least one growth factor or cytokine at a predetermined phase of the cell cycle, wherein:
  - i) the growth factor comprises G-CSF, GM-CSF, or steel factor; and
  - ii) the predetermined phase of the cell cycle is mid-S phase or late S phase;
- c) subculturing the cells until differentiated hematopoietic cells are produced; and
- d) isolating the differentiated hematopoietic cells from the subculture.

26 (withdrawn). A method of treating a subject having cytopenia comprising administering to the subject a therapeutically effective amount of the isolated differentiated hematopoietic cells produced according to the method of claim 25.

27 (withdrawn). A method preventing cytopenia in a subject comprising administering to the subject a therapeutically effective amount of the differentiated hematopoietic cells produced according to the method of claim 25.

28 (withdrawn). Isolated hematopoietic cells produced by the method of claim 25.

29 (previously presented). The method of claim 1, wherein the predetermined phase of the cell cycle comprises a differentiation hotspot.

30 (currently amended). The method of claim 1, wherein the predetermined phase of the cell cycle comprises a reversible differentiation hotspot, wherein a differentiated cell arises from a stem cell.

31 (previously presented). The method of claim 1, wherein the step of contacting of the cells at the predetermined phase of the cell cycle favors a specific differentiation pathway.

32 (withdrawn). A method for the production of cell cycle specific differentiated hematopoietic cells comprising:

a) culturing bone marrow stem cells under conditions that promote synchronous progression through the cell cycle by:

i) providing purified bone marrow stem cells; and

- ii) culturing the purified bone marrow stem cells for cycle initiation from resting state in medium comprising steel factor (FTS), FLT-3 ligand, and thrombopoietin to obtain a culture predominantly comprising synchronous bone marrow stem cells;
- b) contacting the synchronous bone marrow stem cells with an inductive differentiation medium at a predetermined phase of the cell cycle, wherein:
  - i) the predetermined phase of the cell cycle is mid-S phase or late S phase; and
  - ii) the inductive differentiation medium comprises G-CSF, GM-CSF, and steel factor (FTS); and
- c) subculturing the cells until cell cycle specific differentiated hematopoietic cells are produced.

33 (withdrawn). The method of claim 32, wherein the predetermined phase of the cell cycle is mid-S phase and wherein mid-S phase occurs about 32 hours after initiation of the culturing of the stem cells under conditions that promote synchronous progression through the cell cycle.

34 (withdrawn). The method of claim 32, wherein the predetermined phase of the cell cycle is late S phase and wherein late S phase occurs about 40 hours after initiation of the culturing of the stem cells under conditions that promote synchronous progression through the cell cycle.

35 (withdrawn). The method of claim 32, wherein the step of subculturing the cells is carried about for about 14 days.

36 (withdrawn). The method of claim 32, further comprising isolating the differentiated hematopoietic cells from the subculture.

37 (withdrawn). The method of claim 32, wherein the differentiated hematopoietic cells comprise megakaryocytes.

38 (withdrawn). The method of claim 32, wherein the differentiated hematopoietic cells comprise platelets.

39 (withdrawn). The method of claim 32, wherein the differentiated hematopoietic cells comprise proliferative granulocytes.

40 (withdrawn). The method of claim 32, wherein the differentiated hematopoietic cells comprise mature (non-proliferative) granulocytes.

41 (withdrawn). The method of claim 32, wherein the bone marrow stem cells comprise Lineage<sup>negative</sup>Rhodamine<sup>low</sup>Hoescht<sup>low</sup> (LRH) cells.

42. – 53. (canceled)

54 (new). A method for the production of cell cycle specific differentiated hematopoietic cells comprising:



a) culturing purified bone marrow stem cells for cycle initiation from resting state under conditions that promote synchronous progression through the cell cycle;

b) contacting the cells with at least one growth factor or cytokine at a predetermined phase of the cell cycle; and

c) subculturing the cells until cell cycle specific differentiated hematopoietic cells are produced, wherein:

i) the predetermined phase of the cell cycle is mid-S phase and the differentiated hematopoietic cells comprise megakaryocytes, platelets, or proliferative granulocytes; or

ii) the predetermined phase of the cell cycle is late S phase and the differentiated hematopoietic cells comprise mature (non-proliferative) granulocytes.

55 (new). The method of claim 54, wherein the at least one growth factor or cytokine comprises G-CSF, GM-CSF, or steel factor.

56 (new). The method of claim 54, wherein culturing the cells under conditions that promote synchronous progression through the cell cycle comprises culturing the cells in the presence of steel factor, thrombopoietin, and FLT3-ligand.

57 (new). The method of claim 54, wherein the step of subculturing the cells is carried about for about 14 days.

58 (new). The method of claim 54, wherein the predetermined phase of the cell cycle is mid-S phase and mid-S phase occurs about 32 hours after initiation of the culturing of the stem cells under conditions that promote synchronous progression through the cell cycle.

59 (new). The method of claim 54, wherein the predetermined phase of the cell cycle is late S phase and late S phase occurs about 40 hours after initiation of the culturing of the stem cells under conditions that promote synchronous progression through the cell cycle.

60. (new). The method of claim 54, further comprising isolating the differentiated hematopoietic cells from the subculture.

61 (new). The method of claim 54, wherein the predetermined phase of the cell cycle comprises a differentiation hotspot.

62 (new). The method of claim 54, wherein the predetermined phase of the cell cycle comprises a reversible differentiation hotspot, wherein a differentiated cell arises from a stem cell.

63 (new). The method of claim 54, wherein the step of contacting of the cells at the predetermined phase of the cell cycle favors a specific differentiation pathway.

64 (new). The method of claim 54, wherein the bone marrow stem cells comprise Lineage<sup>negative</sup>Rhodamine<sup>low</sup>Hoescht<sup>low</sup> (LRH) cells.